SYNTHESIS OF SULFAMIDOPYRIMIDINES*

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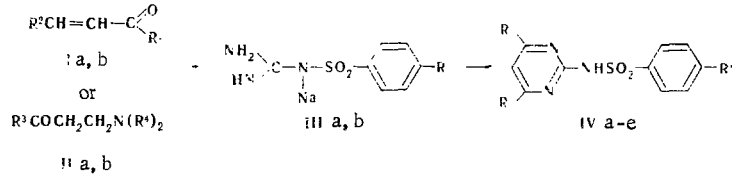
The corresponding pyrimidines are formed in the reaction of α,β-unsaturated carbonyl compounds and Mannich keto bases with amidines and guanidine under dehydration and dehydrogenation conditions (for example, see [2, 3]).

We attempted to use sulfonylguanidines in this condensation, inasmuch as it could lead to the synthesis of 2-sulfamidopyrimidines, which are widely used as antibacterial preparations; however, our attempts were unsuccessful, probably because of the electron-acceptor effect of the SO_2R group. However, when the sulfonylguanidines were converted to the sodium salts, condensation with α,β-unsaturated carbonyl compounds and with Mannich keto bases gave the corresponding 2-sulfamidopyrimidines, which were identical to authentic samples.



I a $R^2=C_6H_5$, $R^3=H$; b $R^2=R^3=C_6H_5$; II a $R^3=CH_3$, $R^4=C_2H_5$; b $R^3=C_6H_5$, $R^4=CH_3$; III a $R^1=NH_2$; b $R^1=CH_3$; IV a $R^1=NH_2$, $R^2=C_6H_5$, $R^3=H$; b $R^1=NH_2$, $R^2=R^3=C_6H_5$; c $R^1=NH_2$, $R^2=H$, $R^3=CH_3$; d $R^1=CH_3$, $R^2=H$, $R^3=C_6H_5$; e $R^1=CH_3$, $R^2=R^3=C_6H_5$

EXPERIMENTAL

2-(4-R-Benzenesulfamido)pyrimidines. A 0.01-mole sample of α,β-unsaturated carbonyl compound (or Mannich keto base) and 4 g of 4A molecular sieves were added to a solution of 0.01 mole of the sodium salt of 4-R-phenylsulfonylguanidine in 15 ml of DMSO, and the mixture was heated at 130-140° for 10 h, during which a stream of dry air was passed through it. Two-thirds of the DMSO was removed by vacuum distillation, the residue was poured into 40 ml of water, and the aqueous mixture was acidified to pH 7 with 5% HCl. The resulting precipitate was removed by filtration, and the pyrimidines were isolated by means of preparative thin-layer chromatography (TLC) on a loose layer of silica gel in chloroform–methanol (95 : 5) (A) and chloroform–dioxane (80 : 20) (B) systems.

*Communication LVIII from the series "Pyrimidines." See [1] for communication LVII.

TABLE 1. Synthesized Pyrimidines

Compound	Starting compounds		mp, °C	TLC system	Yield, %
IVa	Ia	IIIa	261—262	A	12
IVa	IIb*	IIIa	261—262	B	14
IVb	Ib	IIIa	266—268	A	18
IVc	IIa	IIIa	235—236	B	10
IVd†	IIb	IIIb	269—271	A	25
IVe†	Ib	IIIb	228—229	A	27

*The methiodide of IIb was used.

†The results of elementary analysis for C, H, N and S were in agreement with the calculated values.

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SULFOLENES IN REACTIONS WITH SOME 1,3-DIPOLAR REAGENTS

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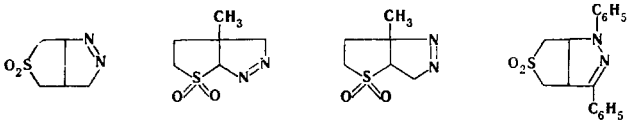
We have shown that 3-sulfolenes (I) and 2-sulfolenes, like other cyclic olefins, are capable of undergoing 1,3-dipolar cycloaddition. Thus at 15-20°C sulfolene I reacts with diazomethane to give II, which is stable on storage and even when it is heated in acetonitrile (at 60° for 7 h). 3-Methyl-3-sulfolene does not react with CH_2N_2. 2-Sulfolene reacts vigorously with CH_2N_2, but the reaction product decomposes rapidly in air. 2-Methyl-2-sulfolene practically does not react with CH_2N_2, whereas its 3-methyl-2-sulfolene isomer forms III in 40% yield. The PMR spectrum of III (in hexametapol) contains a 6-H signal at 6.3 ppm with J = 1.5 Hz. The doublet character is apparently due to the long-range coupling with 3-H or 5-H. The 6-H signal in the spectrum of alternative structure IV should be in the form of a triplet.



II III IV V

3-Oxo-4-methylsulfolene reacts with CH_2N_2 quantitatively to give 3-methoxy-4-methyl-2-sulfolene [1]. 1,3-Diphenylnitrilimine (from benzoyl chloride phenylhydrazone and triethylamine) reacts with sulfolene I to give V.

EXPERIMENTAL

A solution of 2.8 g (0.024 mole) of sulfolene I in 10 ml of dioxane and a solution of 2.7 g (0.071 mole) of CH_2N_2 in ether were mixed. After 13 days, the amorphous flakes were removed by filtration, the filtrate was concentrated, and the crystals were removed by filtration and washed successively with ether and hot benzene to give 3.32 g (90%) of white crystals of 5,5-dioxo-3H-3a,4,6,6a-tetrahydrothieno[3,4-c]pyrazole (II) with mp 129-130°. A similar procedure was used to obtain 1.6 g (34%) of 6,6-dioxo-3H-3a-methyl-3a,4,5,6a-tetrahydrothieno[2,3-c]pyrazole (III) with mp 167-169.5° (from ethanol). The filtrate was worked up to give 1.6 g of starting 3-methyl-2-sulfolene with mp 77-78°. Typical IR spectrum (of a mineral oil suspension, UR-10 spectrometer): 1560 (N=N); 1305-1315, 1115-1150 cm^{-1} (SO_2).

A solution of 2.7 g (0.071 mole) of CH_2N_2 in ether was added in portions at 7-10° to a solution of 3.5 g (0.024 mole) of 3-oxo-4-methylsulfolane in 10 ml of dioxane. After 24 h, the mixture was worked up as in the preceding experiment to give 3.8 g (99%) of 3-methoxy-4-methyl-2-sulfolene with mp 58.5-60° (from ethyl acetate).

A 6-g (0.058 mole) sample of $(C_2H_5)_3N$ was added in a CO_2 atmosphere to a solution of 6 g (0.05 mole) of sulfolene I and 11.5 g (0.05 mole) of benzoyl chloride phenylhydrazone in 100 ml of dioxane, and the mixture was stirred at 15-20° for 2 h and at 60° for 11 h. The precipitated $(C_2H_5)_3N \cdot HCl$ was removed by filtration, and the

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